Sequential CT study of subependymal giant-cell astrocytoma associated with tuberous sclerosis

Case report

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The authors describe the growth pattern of a subependymal giant-cell astrocytoma associated with tuberous sclerosis, which was documented by sequential computerized tomography scans over 7 years. The diagnosis and treatment of this tumor are discussed, and the pertinent literature is reviewed.

KEY WORDS • subependymal astrocytoma • tuberous sclerosis • brain neoplasm • computerized tomography

It is well established that intraventricular tumors occur in association with tuberous sclerosis and that this type of tumor is unique and histologically different from other astrocytomas. It has been called a "subependymal giant-cell astrocytoma." In general, it originates from the subependymal nodule which corresponds to the germinal mantle of the developing brain. This entity has been interpreted as being intermediate between a neoplasm and a heterotopia. Because of the controversy as to whether the basic nature of the lesion is dysplastic or neoplastic, surgical treatment is not well standardized.

In this report, a patient is presented who was followed for 7 years by computerized tomography (CT) before and after the appearance of a tumor of this type. Based on these scans, we were able to demonstrate enlargement of a subependymal nodule in childhood and its subsequent transformation into an astrocytoma. To our knowledge, there is no report dealing with sequential CT study of a subependymal giant-cell astrocytoma.

Case Report

This 12-year-old left-handed boy first experienced generalized tonic-clonic seizures when he was 2 years old and was diagnosed as having tuberous sclerosis. He was born by normal delivery without abnormal gestational or perinatal events, and his family history was negative for neurological disease or consanguinity. He was treated with anticonvulsant therapy. In 1977, at the age of 5 years, he was first evaluated by CT scan on the introduction of the CT scanner to our hospital. There were multiple intracranial calcifications characteristic of tuberous sclerosis (Fig. 1A). Neurological examination at that time was unremarkable except for an adenoma sebaceum and an intelligence quotient of 60. A subsequent plain CT scan, at the age of 7 years, revealed intraventricular nodules protruding from the caudate nucleus to the foramen of Monro (Fig. 1B). The patient was again examined by CT scanning 1½ years later; this revealed a slight increase in the size of the mass at the foramen of Monro, and the other periventricular nodules showed no remarkable change in size (Fig. 1C). Seizures became more frequent and he was treated with a combination of anticonvulsant agents.

At the age of 12 years, the patient began to have headaches which gradually worsened. He developed uncontrollable seizures and became progressively drowsy with nausea and vomiting. A plain CT scan showed a large dumbbell-shaped tumor extending into the left frontal horn, obstructing the foramen of Monro bilaterally and causing hydrocephalus (Fig. 1D). A CT scan after administration of contrast medium revealed marked enhancement of the mass. He was seen at our neurosurgical clinic, and carotid angiography revealed a faint accumulation of contrast medium just above the internal vein on the left (Fig. 2).
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In November, 1983, the tumor was totally removed through a transcortical, intraventricular approach. The mass was sharply defined and highly vascular with blood vessels presenting an angiomatous appearance. It had a broad attachment to the inferolateral wall of the lateral ventricle. Histologically, it was consistent with a typical subependymal giant-cell astrocytoma, and no malignancy was found (Fig. 3). The postoperative course was uneventful and the patient's seizures were completely controlled with medical therapy.

Fig. 1. Unenhanced computerized tomography scans obtained over a 7-year period before and after the occurrence of subependymal giant-cell tumor with tuberous sclerosis. A: Scans at 5 years of age showing multiple intracranial calcifications characteristic of tuberous sclerosis. B: Scans at 7 years of age showing an intraventricular tumor protruding from the caudate nucleus. C: Scans at 8½ years of age showing slight growth of the tumor at the foramen of Monro. D: Scans at 12 years of age showing a large dumbbell-shaped dense subependymal tumor and hydrocephalus.

Fig. 2. Carotid angiogram showing faint accumulation of contrast medium just above the internal vein on the left.

Fig. 3. Photomicrograph of the excised mass showing the morphology of cells in a subependymal giant-cell astrocytoma. The cells, although variable in size, are mainly very large and often exhibit a giant bizarre fusiform or pyramidal form. H & E, × 260.
Discussion

Tuberous sclerosis, originally described by von Recklinghausen in 1862, commonly presents with the features of Vogt’s triad: seizures, mental retardation, and facial adenoma sebaceum. This disorder has an autosomal dominant inheritance involving all three germ layers with resultant neuroectodermal proliferation and early migration and maturatation. The presence of subependymal nodules in the lateral ventricles and cortical tubers is a classical and consistent expression. Calcification often occurs especially in the periventricular region, allowing early diagnosis by CT scan or later by plain skull x-ray films. The CT scan has become indispensable for identification of the intracranial pathology in tuberous sclerosis.

Although the incidence of intracranial calcification increases with age, subependymal giant-cell astrocytomas are relatively rare. Maki, et al., found only one case with neoplastic change among the 60 patients who were diagnosed as having tuberous sclerosis clinically and by CT scan. Subependymal giant-cell astrocytoma is believed to originate from the subependymal tuber, and is histologically different from other astrocytomas and from the tubers found in the cortex. Russell and Rubinstein considered that subependymal giant-cell astrocytoma should be separated from the giant-cell forms of glioblastoma and from the ganglion-cell tumors. They cited the case of a 22-year-old man known to have had a tumor for 17 years. They interpreted it as an intermediate stage between the well-defined neoplasm and the smaller “heterotopia” of tuberous sclerosis. Recently, Bonnin, et al., showed that subependymal giant-cell astrocytoma, especially when associated with tuberous sclerosis, includes cells that are apparently unable to express glial fibrillary acidic protein (GFAP or astroprotein), and suggested that the cell of origin of this tumor was the product of a dysgenetic event in early development. However, they still considered this tumor to be a variant of astrocytoma. Bender and Yunis stated that approximately one-third of the cells were positive for GFAP, including some of the cells they interpreted as neuronal in origin. On the other hand, the cortical tubers did not seem to exhibit a tendency toward tumor formation.

There are some disagreements regarding the therapy of subependymal giant-cell astrocytoma associated with tuberous sclerosis. These tumors do not appear to be highly sensitive to radiation therapy, and they have not been reported as highly invasive tumors in any of the published series. Unfortunately, this tumor is invariably large and often exceedingly vascular by the time it comes to medical attention, despite its benign features. The operative morbidity and mortality are high and many cannot be totally removed. In the report of Painter, et al., two neonates with tuberous sclerosis and giant-cell astrocytoma diagnosed soon after birth developed cardiac arrhythmia and died during surgery. In the series reported by Kapp, et al., three of seven patients with this disorder died and other patients were retarded and required institutionalization.

Eisenberg considered the only indication for operation to be signs and symptoms caused by the mass, usually raised intracranial pressure or hydrocephalus. For those patients without symptoms attributable to the mass, particularly when the tumor is small, he recommended monitoring with CT scanning. Winter also recommended periodic CT scans at least every 2 to 3 years for patients with tuberous sclerosis to detect the development of a glioma. We believe that early surgery should be carried out as recommended by Boesel, et al. They emphasized the possibility of rapid increase of intracranial pressure in these patients. Sequential CT scans of our patient confirmed slow enlargement of the subependymal nodules that eventually resulted in transformation into a diffusely infiltrating astrocytoma. These lesions may occasionally show more aggressive growth characteristics or even massive intraneoplastic intraventricular hemorrhage even though they are benign biologically. The total removal of a subependymal giant-cell astrocytoma increases the chance of relieving intracranial hypertension and achieving prolonged survival.

References

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